Remarks

The Examiner has issued a restriction requirement whereby Applicants are required to elect from the following groups:

Group I, claims(s) 1-8, drawn to a heterologous fusion protein.

Group II, claim(s) 16, 18-19, 25, drawn to a method of treatment of diabetes.

Group III, claim(s) 17-19, drawn to a method of inducing weight loss.

Furthermore, the Examiner contends that the species in the claims are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Applicants elect Group I for the restriction requirement and SEQ. ID. NO. 1 as the elected specie with traverse.

Applicants respectfully disagree with the Examiner in that the species lack unity of invention because the species are not so linked as to form a single general inventive concept under PCT Rule 13.1. The general inventive concept relates to the finding that the problems associated with the potential immunogenicity and effector activity associated with administration of GLP-1-Fc fusions are overcome by identifying specific GLP-1-Fc fusion proteins that have a reduced risk of inducing an immune response after repeated and prolonged administration and no longer have effector function. These specific fusion proteins have substitutions at various positions in the GLP-1 portion as well as the Fc portion of the molecule. The substitutions described herein provide increased potency, increased *in vivo* stability, decreased effector function and decreased immunogenicity.

The Examiner suggests that Glaesner et al. (2002 as disclosed in the IDS) teach a heterologous fusion protein comprising a GLP-1 compound and the Fc portion of an immunoglobin and therefore the claimed invention makes no contribution over the prior art, and consequently there is no special technical feature uniting all of the claimed inventions.

Applicants respectfully disagree. The Fc region has changes intended to minimize immunogenic effector function, to eliminate a potential N-linked glycosylation site and to favor dimerization. Changes have been made to increase plasma half-life and to minimize

immunogenic side effects of this GLP-1-Fc. The C-term of GLP-1 has been changed so as to abrogate a potential immunogenic epitope, position 8 has been changed to inhibit cleavage by dipeptidyl peptidase IV and position 22 has been change to minimize aggregation tendencies. These specific changes in the GLP-1-Fc fusions result in a novel and inventive protein which is useful for the treatment of diabetes and the treatment of obesity.

The Examiner has required restriction between product and method claims. Applicants request consideration for rejoinder of the method claims if Applicants' product claims are found allowable.

If, for any reason, the Examiner feels that a telephone conversation would be helpful in expediting the prosecution of this case, the Examiner is urged to call me.

Respectfully submitted,

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